ANNUAL REPORT

OF

THE HOWE LABORATORY OF OPHTHALMOLOGY

HARVARD MEDICAL SCHOOL

1956

243 CHARLES STREET

BOSTON, MASSACHUSETTS

STAFF

David G. Cogan, M.D.: *Professor of Ophthalmology — Director*
W. Morton Grant, M.D.: *Associate Professor of Ophthalmology*
Jin H. Kinoshita, Ph.D.: *Associate in Biological Chemistry*
David D. Donaldson, M.D.: *Instructor in Ophthalmic Research*
Harold L. Kern, Sc.D.: *Instructor in Ophthalmic Research*
Toichiro Kuwabara, M.D.: *Instructor in Ophthalmic Research*
Robert R. Trotter, M.D.: *Instructor in Ophthalmology*
Thomas Masurat, A.B.
Lorenzo O. Merola, B.S.

TEMPORARILY ATTACHED TO THE LABORATORY

Edward C. Ferguson, M.D.: *U. S. Public Health Service Training Fellow in Ophthalmology*

Kevin Hill, M.D.: *E. B. Dunphy Fellow in Ophthalmic Research*

Jed L. Howard, A.B.: *U. S. Public Health Service Training Fellow in Ophthalmic Research*

Hiroshi Ikui, M.D.: *Research Associate in Ophthalmology Lederle International Fellow*

Maurice E. Langham, Ph.D.: *Instructor in Ophthalmic Research, F. H. Verhoeff Fellow in Ophthalmology*

Pei-Fei Lee, M.D.: *U. S. Public Health Service Fellow in Ophthalmology*

Harvey Lincoff, M.D.: *U. S. Public Health Service Training Fellow in Ophthalmology*

Jeremiah Silbert, A.B.: *U. S. Public Health Service Clerkship*

Sheldon D. Stern, M.D.: *Boston Eye Bank Fellow in Ophthalmology*

Donald P. Tucker, M.D.: *U. S. Public Health Service Training Fellow in Ophthalmology*

Robert C. Watzke, M.D.: *U. S. Public Health Service Training Fellow in Ophthalmology*

THE outstanding event of the past year for the Howe Laboratory has been the transfer of activities to the new Research Building. Occupying one entire floor, the Laboratory now has space that more than doubles that of a decade ago. With the advantages of air conditioning, an attached animal farm and an outstanding machine shop, the Laboratory is a physical unit that may well be the best of its kind in the country. For this and for many other benefactions we are profoundly grateful to the Infirmary.

Although subject to change as opportunities wax and wane, the Laboratory is now divided into overlapping units of biochemistry, pharmacology and toxicology, physiology, experimental pathology, optics (including photography), and clinical investigation. While most of the space is assigned to career investigators, it is hoped to keep some space available for investigators and trainees attached to the Laboratory for short periods of time. The size of the Laboratory is commensurate with the activities of the present staff, but further increase in staff will necessarily require additional space. Such is the restless pace of current research that possibilities for, and the wisdom of, further expansion are already under discussion.

Research Activities*

Ocular hydrodynamics and glaucoma.

In previous years research has been directed primarily toward measurement of outflow from the eye. Quantitative techniques for testing the facility of outflow called tonography were developed by Dr. Grant and are now widely used throughout the world. The result has been a more effective means for diagnosis and evaluation of therapy for glaucoma, as well as a clearer concept of the basic factors responsible for intra-ocular fluid dynamics in health and disease.

Research of the past year on intra-ocular fluid dynamics has to some extent extended these techniques but has been

* It is with some pride that the Howe Laboratory views two awards of the past year. One is the Proctor Award given to Dr. Grant by the Association for Research in Ophthalmology for his many contributions in ophthalmology. The other is the Lasker Award to Dr. V. Everett Kinsey, now of the Kresge Eye Institute and formerly of the Howe Laboratory, given by the Albert and Mary Lasker Foundation for his studies on retrolental fibroplasia.

especially concerned with new approaches which are still in the process of trial and evaluation.

Preliminary observations have been made of the electrical potential across the blood aqueous barrier to determine the relationship of this potential to the formation of aqueous humor.

The effect of calcium phosphorylcholine chloride and several other organic quaternary compounds on intra-ocular pressure was examined because of published reports suggesting that this phosphorylcholine has the interesting and unusual property of raising the intra-ocular pressure in rabbit and human eyes. It was disappointing to find that this substance actually did not raise the pressure in normal human eyes and that its effect in rabbit eyes was only that of the calcium chloride contained in the molecule, an action recognized many years ago. Other quaternary ammonium compounds were found to cause miosis in accord with recognized relationships between chemical structure and parasympathomimetic activity, but no significant additions were found for the anti-glaucoma armamentarium.

Exploratory studies on mechanisms which tend to stabilize intra-ocular pressure were initiated last year, and further research in this field has been undertaken. Experimental analysis of physiologic control of intra-ocular pressure has been pursued in this Laboratory in various ways for many years, but these most recent investigations constitute a new departure. They were instigated because of interest in possible homeostatic mechanisms by Charles Rife, M.D., who took over the techniques developed by Dr. Grant for measurement of ocular pressure, volume and flow by means of electronic strain gages. Dr. Rife improved and extended these techniques and initiated an experimental program for study of the manner in which aqueous formation and outflow respond to variations in intra-ocular pressure.

Unfortunately, this work was interrupted for several months when the Howe Laboratory moved to new quarters, and when Dr. Rife took up his duties as an ophthalmic resident at the Massachusetts Eye and Ear Infirmary. Now, however, the program has been reactivated and expanded by Maurice Langham, Ph.D., a physiologist who is visiting this laboratory for a year as the first Verhoeff Fellow. Dr. Langham has already become well known in ophthalmology for his work on mechanism of action of Diamox on intra-ocular pressure as

well as for other ophthalmo-physiologic studies which he carried out as a member of the Eye Institute of London. The exceptionally good facilities at the Howe Laboratory for experimental study of intra-ocular pressure have been made available to Dr. Langham. With advice from Dr. Rife, Dr. Langham has taken up the study of physiologic factors which govern intra-ocular pressure and appears to have established the presence of a homeostatic mechanism acting to keep the pressure within narrow limits. Current investigations include a study of neurological factors which could modify this homeostatic mechanism and a study of possible effects transmitted from one eye to the other.

The possibility that the pressure lowering effect of carbonic anhydrase inhibitors, such as Diamox, is related to their speed of entry into the eye, is being tested by Dr. Langham. This problem is of importance in the elucidation of how carbonic anhydrase inhibitors reduce the intra-ocular pressure and also in obtaining suitable compounds for clinical use.

Clinical investigations of glaucoma have largely been shifted to the Glaucoma Consultation Service which has been an outgrowth of the Howe Laboratory's researches and which will be described subsequently in this Report.

Fat formation in the eye and other tissue

Studies on fat formation in the cornea and other tissues have led to several intriguing conclusions. The phenomenon with which Drs. Cogan and Kuwabara have been concerned, called "aberrant lipogenesis" to distinguish it from normal fat formation, occurs only in the presence of serum and an oleate-containing substrate. The serum factor contains several essential components which have been incompletely identified. Oleate or an oleate-containing compound, on the other hand, is the exclusive substrate which will support lipogenesis in the presence of serum, and it seems altogether probable that so-called fatty degeneration in general depends on the native oleate of body lipids. As far as the cells are concerned, aberrant lipogenesis is an intra-cellular, enzymatic process that is found in many, but not all, cells of the body. Thus it is abundant in the cornea, liver, and some kidney tubules but absent in brain tissue, polymorphonuclear cells, most striated muscle, and some other tissue. The heart is a special case showing highly selective lipogenesis by different muscle fibers. Current in-

vestigations are directed toward the cardiovascular implications of aberrant lipogenesis and toward identification of the fat formed.

The results of these studies are to be reported shortly in a journal of general pathology. Their ultimate importance can be evaluated only with time, but that it will transcend the strictly ocular aims which prompted the studies originally seems reasonably certain. Just as knowledge of the eye gains much from research on tissues elsewhere in the body, it is hoped that knowledge of general tissue reactions may be better understood through research directed primarily to the eye.

Biochemistry of the lens and cataracts

Interest in the sulfhydryl (–SH) compounds found in lens stems from the possible influence of these reactive groups on the state of lens protein. It is known that a decrease in glutathione, a sulfhydryl compound normally present in high concentrations in lens, is one of the earliest changes observed in the process of experimental cataract formation. There is also the suggestion that the conversion of protein sulfhydryl groups to disulfide linkages is a factor which may be important in affecting the transparency of the lens. Because of a possible significance in cataract formation, Dr. Kinoshita and his group are making a systematic study of these sulfhydryl compounds in the bovine lens. There appear to be 50 micromoles of sulfhydryl groups per gram of fresh weight of lens. Of this amount there are 10 micromoles of glutathione per gram indicating that there are four times more protein sulfhydryl groups than glutathione. However, as demonstrated in homogenates of lens, the sulfhydryl groups of glutathione appear to be much more reactive than the protein sulfhydryls. Alkylating agents, such as N-ethylmaleimide, react much more readily with glutathione than with protein –SH. Oxidation of glutathione, catalyzed by cupric ions, occurs much more readily than oxidation of the protein –SH. The lower reactivity of the protein –SH may be due in part to "masking" by hydrogen bonds. The "unmasking" of the lens protein –SH by treating with concentracted urea solution markedly increases the reactivity of the protein –SH groups.

The reactivity of the –SH groups of glutathione depends greatly on whether the experiments are carried out on whole lens or on lens which has been homogenized. The glutathione

contents of intact and homogenized lenses are compared after storage at 5°C in isotonic buffer solution. After 24 hours of storage in the cold, only a small amount of glutathione is detectable in the homogenized lens. On the other hand the glutathione of the intact lens is decreased by only 20–30% of the original value even after 48 hours' storage in the cold. In both cases it can be shown that the glutathione which disappeared can be recovered as the oxidized form. It appears that the oxidation which is the result of an interaction of two glutathione molecules readily takes place in homogenates but not in intact lens. The explanation of this may be that the glutathione in the intact lens is not freely diffusible. This view is consistent with other observations made on the extractability of lens glutathione. Extraction of glutathione was studied by incubating lens in a buffer solution and determining the amount of glutathione which diffused out. On incubating lens up to four hours, the maximal amount of glutathione extractable was 20% of the original value. Altering the pH from 5.5–8.0 did not influence the extractability of glutathione. However, glutathione was readily extractable from lens when incubated in concentracted urea or guanidine solutions. The effect of these solutions does not seem to be due to its hypertonicity because the same concentraction of glucose or sodium chloride solutions had no such effect. These results suggest that most of the glutathione is held to the lens protein by hydrogen bonding and the action of urea and guanidine solutions is to release glutathione by disrupting this type of bond.

Toxicology and the cornea

This is a continuing project, previously described in these Annual Reports, in which biological studies carried out by Dr. Grant are correlated with chemical studies carried out by Dr. Kern. These investigators have determined that many metal cations interact with carboxyl groups (chiefly the mucoprotein fraction) of the corneal stroma at neutrality. They found that some metals interacting in this way did not appreciably alter or damage the cornea, but that certain other metals greatly reduced the capacity of the tissue to absorb water and rendered the mucoproteins insoluble. These physical changes were found to be associated with gradual opacification of the cornea in the eyes of live animals. In some instances the derangement of water absorption and mucoprotein solubility

was found to be reversible by use of antidotes which remove the metal cations from their combination with the tissue. In these instances the development of corneal opacification proved to be largely preventible by timely treatment.

With the ultimate aim of finding effective means for treatment of still other chemical injuries of the cornea, Drs. Grant and Kern have been attempting to discover the general principles which govern the toxicity of ionic substances to this tissue. They have found an apparent correlation between toxicity and unusual affinity or tenacity of binding of metals by the cornea. However, some probable exceptions to this correlation have necessitated considering the possibility that all metals do not interact with the same groups in the cornea, but that some may interact selectively with special groups, and that the identity of the groups involved, as well as the strength of binding, may govern the injuriousness of the reaction. This complex problem has been attacked by means of polarographic and spectrophotometric methods for study of the interactions of metals with the cornea and for examination of competitive influences of metals on one another in interaction with the cornea. At the present status of this work it appears that the deleterious influence of certain metals, particularly the lanthanons or rare earth metals, is attributable to the formation of a very strong and persistent bond between these metals and those carboxyl groups in the tissue with which the alkali and alkaline earth metals also interact. The injuries induced in this case do not appear to be attributable to a selective interaction with special chemical groups. On the other hand, the alkali metals and most of the alkaline earths, although interacting with the same groups as the lanthanons, form weak and easily dissociable bonds, and cause no serious disturbance of the physical or vital properties of the cornea. Certain other metals, such as copper, beryllium and manganese, have only moderate affinity for these same groups in the cornea, yet cause considerable injury. In this instance we have evidence that these metals interact selectively with groups in the tissue other than those which bind the innocuous alkali and alkaline earth metals. Whether in this instance it is again the strength of bond or possibly a peculiar critical nature of the special groups involved which is responsible for the injurious effect remains to be ascertained.

As further part of the study of interaction of ions and the

cornea, a series of quaternary ammonium salts and a series of cationic and anionic dyes have been tested for toxicity on the corneas of rabbits, and the effects of these substances on the physical properties of the tissue have been examined. The dyes have been studied chromatographically to ascertain their composition, and now continuous flow electrophoresis is being employed to purify some of the dyes for quantitative chemical study of their interactions with the cornea. Examination of the toxicity and chemical reactivity of the series of quaternary ammonium salts has indicated that injuriousness to the cornea in this case is related to physical attributes of the molecules, as manifested in surface-tension-lowering effect, rather than to chemical affinity for the carboxyl groups of the cornea.

Apart from the study of toxicity of ions to the cornea, Dr. Grant has been exploring a new possibility for relieving the miosis and spasm of accommodation which are caused by phosphate-derived cholinesterase inhibitors such as the drug DFP, the insecticide TEPP, and the war-time nerve gases. Established treatment has been based on administration of atropine to block the action of the acetylcholine which is in excess, but a satisfactory balance between these antagonists is difficult to achieve. The new treatment which is being explored is an attempt to exploit the development by Irwin Wilson of Columbia Medical School of a substance known as PAM which actually reactivates poisoned cholinesterase enzyme to restore natural conditions. Dr. Grant has established that the substance does overcome the miosis of DFP when administered locally, but whether it is feasible to apply it to human eyes we have not yet established.

Radiation and the eye

The ocular effects of radiation have occupied a prominent place on the Laboratory's agenda for some years. These studies, including notably the action spectrum of ultraviolet keratitis and the cataractogenic properties of ionizing radiation, have been concerned with widely disparate portions of the electromagnetic spectrum. During the past year Drs. Cogan and Donaldson have participated in a project of the Harvard Medical School and the Massachusetts Institute of Technology (Lincoln Laboratories) for study of health hazards of microwaves. This form of radiation, situated in the spectrum between infra-red and radio waves, is rapidly coming into

prominence because of potentially limitless increase in power output of radar installations and because of the increasing use of diathermy for domestic and medical purposes.

Cataracts have reportedly resulted from local exposure of the head and eye region to microwaves. Our particular concern has been with the cataractogenic or other ocular effects from radiation of the entire body such as might occur in the vicinity of a transmitter. To date we have detected no deleterious effect in animals which have survived the irradiation even though the dosages used included the immediately sublethal range and despite the fact that these doses were applied repetitively over several months.

If further experiments now in progress bear out the foregoing experience, we may conclude that there is no local hazard to the eye with whole-body microwave irradiation short of the lethal dosage. Since this intensity is unlikely to be present except in the immediate vicinity of a radar antenna and since the heat from this intensity would adequately warn an exposee that he is being irradiated, microwaves probably do not present the subtle danger comparable to that of ionizing radiations which cause keratitis and cataracts. Moreover, there is apparently no especial vulnerability for damage to the eyes. These conclusions do not, of course, apply to exposures limited to the head or eye region.

Miscellaneous researches

Projects undertaken by persons temporarily associated with the Laboratory are usually aimed at obtaining a specific answer in a short period of time. The selection of the project is often determined by contact with some patient's particular problem. Thus, one study undertaken by Dr. Donald Tucker dealing with the inheritability of retinoblastoma was actually prompted by the question of a young woman who, having had one eye removed for retinoblastoma as a child, wanted to know what her chances were of having children with the same disease. This type of tumor is known to occur in families as a mendelian dominant trait but no satisfactory information could be found in the literature dealing with the inheritance in "sporadic cases" (where neither parent was involved) such as this young woman represented. Accordingly, Dr. Tucker culled from the records of the Infirmary a substantial number of histories on "sporadic cases" of more than 20 years ago. Many of these

erstwhile patients had grown up and had children of their own. Dr. Tucker was able to establish a group of pedigrees of these latter leading to the conclusion that patients with the sporadic occurrence of retinoblastoma had one chance in four of transmitting the disease to 40–50% of their offspring.

Others temporarily associated with the Laboratory have chosen to undertake studies which would utilize the extensive reservoir of case records which have been cross referenced in the Howe Laboratory for these past 20 years. One such study was undertaken by Dr. Harvey Lincoff who, as a Heed Fellow, defined what might be called a pseudo-aneurism syndrome. The sudden onset of third nerve paralysis and pain in the homolateral face occurs so frequently with intracranial aneurism that many cases masquerade under this diagnosis when in fact the underlying cause is other than aneurism. Alternative causes for this syndrome were found to be diabetes, paraclinoid tumor, and ophthalmoplegic migraine.

Another project based on the Laboratory's case records was an attempt by Dr. Edward Ferguson to determine the significance of sparing of the pupil in otherwise complete third nerve palsies. Such cases were found to have in common a localization of the lesion to the posterior orbit or immediately retro-orbital region but to have no one cause in common.

Other investigators temporarily associated with the Laboratory have chosen to pursue studies along more experimental lines. Sudanophilia of the guinea pig cornea following irradiation by x-rays is being studied by Dr. Henry Ring. These studies resulted from a chance observation that, following irradiation, guinea pig corneas developed a lipid that was microscopically visible throughout the collagenous framework of the cornea. This has suggestive similarity to arcus senilis but its further significance is obscure.

A somewhat more comprehensive study is being carried on by Dr. Kevin Hill who, as the first E. B. Dunphy Fellow, is exploring the possibility of cultivating corneal cells in the test tube and of using this means for various physiologic and pathologic studies not possible in the intact organ. Dr. Hill has been particularly concerned to date with the factors responsible for fat formation in cultured corneal cells and hopes to find a way of controlling fat formation on a large scale by varying the nutrient media.

A comparative study of the corneal permeability for various

cortisone derivatives has been carried out by medical student Jeremiah Silbert during his summer vacations. This problem turned out to be frustratingly difficult because of the relative insolubility of the steroids and because of their hydrolysis during the test period. It is not, therefore, planned to pursue these observations further at preseent.

The possible efficacy of gamma globulin for the treatment of herpetic (simplex) iritis is being tested experimentally by Dr. Henry Allen and Mr. Jed Howard. It is as yet too early to evaluate the results.

Measurement of corneal thickness by a device based on the principle of the heliometer was developed in the Howe Laboratory by Dr. Donaldson several years ago but temporarily abandoned for lack of equipment and time. In a revised form, the apparatus is now being evaluated by Dr. Robert Watzke.

Over a period of several years, photographs have been made of the eyes of twins with the aim of distinguishing between genetic and acquired characteristics of the eyes. So far, 70 sets of twins, fraternal and identical, have been photographed and the data is now being analyzed by Dr. Arthur Steinberg from the point of view of a geneticist. This continuing study under the supervision of Dr. Donaldson has had many collaborators of whom Dr. Sheldon Stern was particularly noteworthy during the past year.

Teaching

If the definitive history of the Howe Laboratory should ever be written, one chapter might well be entitled "Adventures in Education". The Laboratory has had an opportunity to pioneer in several aspects of this important field and in some measure to set a pattern that has been found generally useful. Perhaps most notable is the Basic Science Course which was established by the Laboratory almost twenty years ago. The first of its kind in this country and possibly in the world, it was the prototype of many such courses now given throughout the country and has thus had far reaching effects on the current training of ophthalmologists. The course is now ably directed by Dr. Henry Allen, but the Howe Laboratory staff continues to participate actively in the teaching especially in the fields of physiology, biochemistry, pharmacology and toxicology. One departure from precedent during the past year was the incor-

poration of histochemistry into biochemistry thus permitting a more direct illustration of biochemical principles in tissue metabolism and a more effective correlation of biochemistry, anatomy, and pathology. This approach will be further expanded in the coming year.

Perhaps the greatest event during the past few years in ophthalmic education has been the active support of trainees by the Public Health Service. Whereas formerly individuals desiring more than the medical school and residency training have had to rely on very few fellowships or on their own resources, the Public Health Service now gives support to qualified individuals as well as block grants to institutions for training. This impetus to postgraduate education is expected to have far-reaching consequences in the training of ophthalmologists especially in the academic disciplines. The Howe Laboratory has accepted trainees to the limits of its physical facilities and resources. The Director of the Howe Laboratory served as the chairman of the first Training Grants Committee for Ophthalmology of the Public Health Service and continues as a Council member of the National Institute for Neurological Diseases and Blindness. The present policy of maintaining complete freedom for the institutions to execute their programs as they see fit is aimed at most nearly duplicating the conditions of private support, and it can be said to the credit of the Public Health Service that reliance is placed most heavily on civilian advisory boards.

A new adventure during the past year for the Howe Laboratory and for the Ophthalmic Pathology Department with which it is closely associated was the acceptance of an undergraduate medical student for a year's training during the middle of his medical school career. It is expected that this contact with ophthalmology and ophthalmic research may greatly enhance what is derived from the subsequent medical school and general hospital training and, it is hoped, more than compensate for the temporary setback of one year in the school standing. An incidental but important by-product is what he, the student, will have to offer over and above the average experience to his colleagues in the next few years. The Howe Laboratory has participated enthusiastically in this experiment with undergraduate education but the credit for initiating it was due the candidate himself.

Falling within the general sphere of education and the

activities of the Laboratory during the past year was the organization of the first meeting of ophthalmic biochemists. This growing group of active investigators has contributed richly to ophthalmic research during the past few years but has, it was felt, suffered from lack of integration. A two-day conference under the chairmanship of Dr. Jin Kinoshita was therefore called at the Harvard Faculty Club where approximately 25 persons identified with ophthalmic biochemistry met for scientific discussion of their respective studies. This was purposely limited to a small group from the East Coast and Mid-West and aimed at recapturing the informality which so many of the larger meetings have lost. All concerned endorsed the purposes and accomplishments of the meeting enthusiastically. It is to be repeated again this coming year and may well be the anlage of an annual event.

A two-week course in ophthalmic neuro-anatomy and neuro-ophthalmology was given last March by Drs. Donaldson and Cogan at the Clinical Center of the National Institutes of Health in Bethesda, Maryland. This was the first time this course has been given in its entirety outside the sphere of the Harvard Medical School's postgraduate course. Excerpts of this course were also given in Kansas City and Denver.

Falling perhaps within the sphere of teaching and certainly within that of education (for the author, at least) is the revision of the Neurology of the Ocular Muscles which was published this past year. This revision by Dr. Cogan has attempted to incorporate and to evaulate the many new observations in the active field of neuro-ophthalmology.

Service Activities

The perennially difficult task of separating research from service functions is particularly difficult in the case of photography, for Dr. Donaldson's development of photographic techniques has followed, and depended on, his extensive researches in optics. Yet the net result has been one of great service for documentary and teaching purposes and hence is presented here.

Assisted by many persons but particularly in the past year by Drs. Sheldon Stern and Robert Watzke, Dr. Donaldson has continued his collation of stereoscopic slides illustrating a vast array of ophthalmologic conditions. Some 500–600 special

cases have been selected for detailed write-up and discussion. In addition a group of almost 200 stereophotographs representing various anterior segment diseases has been organized specifically for use in teaching the Harvard Medical students. To relieve the congestion in the Howe Laboratory, these slides along with stereoviewers, histories, and discussions have been deposited in the Howe Library in a special area set aside for this purpose.

A new method has been developed for photographing the angle of the anterior chamber in color. A special set of these goniophotographs, as they are called, has been assembled to illustrate the most important aspects of clinical gonioscopy. The set is composed of 33 slides, an atlas, and stereoviewer. About 40 of these sets have been made available, at cost, to various individuals and institutions.

The Glaucoma Consultation Service which is an outgrowth of Drs. Grant's, Chandler's, and Trotter's studies and which operated in its formative period in the Howe Laboratory, has now shifted to the Eye Clinic and is under the supervision of Dr. Trotter. In some instances the house officers who have been attached to this service primarily for training purposes have taken advantage of the opportunity presented to them to carry out limited clinical research studies. On the other hand, the first full-time investigation which has been undertaken in conjunction with the Glaucoma Service since its official inauguration was initiated in mid-1956 by a full-time research fellow supported through the Howe Laboratory by the National Institute of Neurological Diseases and Blindness. Dr. Pei-Fei Lee, recipient of this fellowship, has undertaken under the supervision of Dr. Trotter a systematic gonioscopic and tonographic study of patients before and at various intervals after operation for cataract. Dr. Lee has already observed a number of clinically significant phenomena related to the occurrence of subnormal pressure as well as to the development of glaucoma in these patients. Dr. Trotter, in addition to supervising the activities of the Glaucoma Consultation Service, has become Assistant to the Chief of Ophthalmology, and he is bending his efforts particularly to increasing the overall efficiency of the Eye Clinic.

The Howe Library and the Pathology Department are now administered separately from the Howe Laboratory, but both have close operating ties with it. The Library under the able

stewardship of Mr. Charles Snyder is a model of service. The Pathology Department is now in full charge of Dr. Taylor Smith who effectively combines his clinical talents and academic interests in the field of ophthalmic pathology.

Organization and Support

The Howe Laboratory is the crossroads of diverse interests. Full-time and part-time investigators, medical school staff, hospital staff, and patients—all who have an interest in the eye—have a potential place in the Laboratory. Here, it is hoped, is a profitable meeting of clinical and basic scientists and a dedication of time and effort to the common good. Any problem pertaining to the eye, whether applied or theoretical, has a place in the Laboratory within the limits of physical facilities, available talent, and means for support.

Gifts to the Howe Laboratory go directly to the support of eye research. Overhead and some incidental expenses are covered by long-standing arrangements with the Massachusetts Eye and Ear Infirmary. A division of the Harvard Medical School and copartner of the Infirmary, the Laboratory has no other fostering agency and no other fund raising representation. It has depended on a limited endowment and increasingly on the beneficence of individuals, lay and professional, and on public and private organizations which have chosen to invest in ophthalmic research through the Howe Laboratory. We like to think of ourselves as operating a public trust devoted to research on the eye and that the quality of research and efficiency of operation will be sufficient criteria for attracting support without direct solicitation. It is therefore with great satisfaction and gratitude that we are able each year to list a sizable group of benevolent individuals who have included the Howe Laboratory in their charities.

For general expenses:

Anonymous
The Massachusetts Eye and Ear Infirmary
William P. Beetham, M.D.
Harry E. Braconier, M.D.
Virgil G. Casten, M.D.
Thomas Cavanaugh, M.D.
Mr. Paul C. Cabot
(in memoriam: Henry D. Sedgwick)
Paul A. Chandler, M.D.
Julian F. Chisholm, Jr., M.D.
Thomas P. Cronin, M.D.
William F. Donoghue, M.D.
Edwin B. Dunphy, M.D.
Charles Dyson, M.D.
E. C. Foote, M.D.
Mr. Isaac Futterman
Dr. J. Austin Furfey
Linley C. Happ, M.D.
Miss H. Louise Harris
Carl C. Johnson, M.D.
Mr. Meyer Kestnbaum
Merrill J. King, M.D.
Sumner D. Liebman, M.D.
Henry A. Mosher, M.D.
Estate of Belletta Olsen
Abraham Pollen, M.D.
Marvin Posner, M.D.
Mrs. Murray A. Potter
Miss Dorothy Rogers
Benjamin Sachs, M.D.
David H. Scott, M.D.
Earl S. Seale, M.D.
Mr. William N. Stevenson
Garrett L. Sullivan, M.D.
Mr. J. M. Ulmer

For studies on corneal research:

Boston Eye Bank
Mrs. H. Philip Patey

For studies pertinent to the ocular effects of diabetes:

Anonymous

For training purposes:

For studies on tonography of the eye:

For studies on toxicology of the eye:

For studies of eyes in identical and fraternal twins:

U. S. Public Health Service

For studies on metabolism of the ocular lens:

U. S. Atomic Energy Commission

For studies on intra-ocular fluids and glaucoma:

The Alfred P. Sloan Foundation
Mrs. Frederick H. Lovejoy

For studies on fat metabolism in the cornea and aging processes as reflected in the cornea:

The Massachusetts Heart Association
The American Heart Association

David G. Cogan, M.D.
Director

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with Grant, W. M. (see Grant, W. M.).

Kinoshita, J. H.

with Cogan, D. G.; Kuwabara, T.; Sudarsky, D. and Ring, H. (see Cogan, D. G.).

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Snyder, C.

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Book review: Acta XVII Concilium Ophthalmologicum 1954, Canada, United States of America. Three volumes, cxxxix, 2090 pages. Toronto, University of Toronto Press, 1955. A. M. A. Arch. Ophth. 56: 319–320, August, 1956.

Trotter, R. R.

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with Grant, W. M. (see Grant, W. M.)

Glaucoma Consultation Service. "The News", Massachusetts General Hospital, no. 160: 3–4, October, 1956.

Zeavin, B. H. and Wald, G.

Rod and cone vision in retinitis pigmentosa. Am. J. Ophth. 42: 253–269, October (pt. II), 1956.

LECTURES

COGAN, D. G.

Neurology of the ocular motor system. Series of lectures at the Clinical Center of the National Institutes of Health, in Bethesda, Maryland, March 5–16, 1956.

Eye pathology. Harvard Medical School, Department of Pathology, in Boston, Massachusetts, March 23, 1956.

Ocular fundus. Postgraduate Course in Cardiology, Massachusetts General Hospital, in Boston, Massachusetts, March 27, 1956.

Neuro-ophthalmology. Lectures to the Postgraduate Course in Opthalmology and Otolaryngology of the University of Kansas School of Medicine, in cooperation with the Kansas City Society of Ophthalmology, the Kansas Medical Society, and the Kansas State Board of Health. At the University of Kansas Medical Center, in Kansas City, Kansas, April 9 and 10, 1956.

Some neuro-ophthalmic syndromes. Colorado Ophthalmological Society, in Denver, Colorado, April 11, 1956.

with Kuwabara, T.; Kinoshita, J. H.; Sheehan, L. and Merola, L. Ocular cystinosis in the adult. Presented by Drs. Sheehan and Kinoshita at the Alumni Association Meeting of the Massachusetts Eye and Ear Infirmary, in Boston, Massachusetts, April 17, 1956.

Some ocular manifestations of systemic disease. U. S. Naval Hospital, in Newport, Rhode Island, May 15, 1956.

Spasm of the near reflex. Talk to Eastern Regional Meeting of the American Association of Orthoptic Technicians at the Massachusetts Eye and Ear Infirmary, in Boston, Massachusetts, May 25, 1956.

House Officer Lectures, Massachusetts Eye and Ear Infirmary.

Histochemistry. January 17, 1956.
Eye signs in brain stem and cerebellar disease. June 26, 1956.

DONALDSON, D. D.

Medical stereophotography. Talk to Biological Photographers Association, in New York City, New York, January 26, 1956.

Ophthalmic neuro-anatomy. Clinical Center of the National Institutes of Health, in Bethesda, Maryland, March 5–9, 1956.

Unusual conditions of the anterior segment. Ophthalmological Round Table, in San Francisco, California, September 7, 1956.

House Officer Lectures, Massachusetts Eye and Ear Infirmary.

Lesions of the conjunctiva and iris. January 19, 1956.
Pathology in the angle of the anterior chamber. February 9, 1956.
Lid lesions. May 1, 1956.
Cataracts. July 24, 1956.

Grant, W. M.

Tonography. Colorado Ophthalmological Society, in Denver, Colorado, April 11, 1956.

Current status of tonometry. Alumni Association Meeting of the Massachusetts Eye and Ear Infirmary, in Boston, Massachusetts, April 17, 1956.

Participated in the Josiah Macy Jr. Foundation Conference Program, Second Symposium on Glaucoma, in Princeton, New Jersey, December 3–5, 1956.

Kern, H. L.

with Grant, W. M. Binding of cations to the corneal stroma. Presented by Dr. Kern at the First Conference on Ophthalmic Biochemistry, in Cambridge, Massachusetts, Febrary 11, 1956.

Kinoshita, J. H.

Studies on the glutathione in lens. Presented at the First Conference on Ophthalmic Biochemistry, in Cambridge, Massachusetts, February 11, 1956.

Carbohydrate metabolism of lens. Seminar at Biochemical Research Laboratories, Massachusetts General Hospital, in Boston, Massachusetts, May 1, 1956.

Langham, M. E.

Action of Diamox on normal and glaucomatous eyes. Staff Meeting of the National Institute for Neurological Diseases and Blindness, National Institutes of Health, in Bethesda, Maryland, November 19, 1956.

Some research problems in ophthalmology. Talk to Naval Dentists, in Boston, Massachusetts, October 1956.

Participated in the Josiah Macy Jr. Foundation Conference Program: Second Symposium on Glaucoma, in Princeton, New Jersey, December 3–5, 1956.

Trotter, R. R.

Evaluation of cyclodiathermy as an antiglaucoma procedure. Alumni Association Meeting of the Massachusetts Eye and Ear Infirmary, in Boston, Massachusetts, April 17, 1956.

Glaucoma. Association of Surgeons of the New York Central System, in Boston, Massachusetts, October 3, 1956.

Demonstration of after-image testing device. Talk to Eastern Regional Meeting of the American Association of Orthoptic Technicians at the Massachusetts Eye and Ear Infirmary, in Boston, Massachusetts, May 25, 1956.

FORM OF BEQUEST

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For the information of those who may wish to contribute to this Laboratory, a form of bequest is here set forth:

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